ORIGINAL ARTICLE

Symptomatic change and gastrointestinal quality of life after pancreatectomy

Lewis Rashid & Vic Velanovich*

Division of General Surgery, Henry Ford Hospital, Detroit, MI, USA

Abstract

Background: Pancreatectomy affects gastrointestinal (GI) symptoms. Our purpose was to assess the quality of life of pancreatectomy patients in relation to GI function.

Methods: Pancreatectomy patients were asked qualitative, open-ended questions about symptoms. They also completed the Gastrointestinal Symptom Rating Scale (GSRS) for reflux syndrome, acute pain syndrome, indigestion syndrome, diarrhoea syndrome and constipation syndrome.

Results: A total of 52 patients participated. Of these, 69% reported an improvement and 31% reported no change in preoperative symptoms. No patients reported a worsening of symptoms. Half (50%) of the patients experienced new, different symptoms. Median GSRS scores were 0 for reflux syndrome [inter-quartile range (IQR): 0–1.0], 0 for acute pain syndrome (IQR: 0–1.0), 2.0 for indigestion syndrome (IQR: 1.0–4.0), 2.0 for diarrhoea syndrome (IQR: 0.5–4.5), and 0 for constipation syndrome (IQR: 0–1.0). Whipple operation patients scored higher on the reflux syndrome (0.5 vs. 0; $P = 0.08$) and indigestion syndrome (3.5 vs. 1.5; $P = 0.06$) domains. A total of 68% of Whipple operation patients experienced new symptoms, compared with 32% of patients who had undergone other types of pancreatectomy ($P = 0.002$). Scores of patients who had undergone surgery <2 years and >2 years earlier, respectively, did not differ.

Conclusions: Patients who underwent pancreatectomy frequently experienced an improvement in preoperative symptoms, but also experienced new postoperative symptoms. This was more common after Whipple operations. However, these symptoms were relatively mild in severity. These mild symptoms seem to persist over time.

Correspondence

Vic Velanovich, One Tampa General Circle, Tampa General Hospital, F145, Tampa, FL 33601, USA. Tel: + 1 813 844 4005. Fax: + 1 813 844 7396. E-mail: vvelanov@health.usf.edu

Introduction

In the event of a diagnosis of a benign or malignant tumour of the pancreas, a very limited number of treatment options must be considered and pursued in order to successfully treat the patient. In the USA in 2009, 42 470 individuals were diagnosed with pancreatic adenocarcinoma, for which survival rates at 5 years are only 20% in patients with a localized tumour and are substantially worse in those with more advanced disease.[1] Surgical resection,

*Present affiliation: Division of General Surgery, University of South Florida, Tampa, Florida.

This paper was presented at the 52nd Annual Meeting of the Society for Surgery of the Alimentary Tract, 6–10 May 2011, Chicago, Illinois.

in operable cases, is the primary treatment modality. Although postoperative mortality rates have improved, morbidity remains relatively stable.[2] Postoperative morbidity and mortality rates have rightly received a great deal of attention, but it should be noted that pancreatectomy itself can significantly alter gastrointestinal (GI) physiology.[3,4] These effects result from both decreased pancreatic enzyme and biliary excretions, and the impairment of the endocrine pancreas function as evidenced by statistically significant increases in fasting glycaemia and decreases in C-peptide and insulin levels, potentially resulting in an increased risk for diabetes-specific consequences.[5] This major reduction in metabolic capacity, as well as impacting the physiology of patients, may also affect their quality of life (QoL) by forcing them to make dietary alterations and limiting the extent of interpersonal social

participation and activity. The main focus of this study was to assess the extent to which these alterations impact on patients' everyday lives and to determine which areas will be most affected. The ultimate goal is to be able to better inform and counsel patients as to what is to be expected following these types of operation.

Materials and methods

This study was approved by the Henry Ford Hospital Institutional Review Board.

Inclusion criteria defined participants as patients who had undergone any type of pancreatectomy for benign or malignant tumours and whose surgery had been conducted ≥1 year previously. Patients who had been operated upon for malignant disease were required to exhibit no evidence of recurrence as acknowledged by a review of their most recent medical records. Exclusion criteria excluded patients in whom surgery had been conducted <1 year previously, patients who continued to receive antineoplastic chemotherapy or radiotherapy, patients who underwent debridement for pancreatic necrosis caused by acute pancreatitis, and patients who had been operated upon for pain related to chronic pancreatitis.

Demographic data obtained included age, gender, type of pancreatectomy and pathology. We did not gather information on past medical history, the use of adjuvant chemotherapy or radiation therapy during the treatment protocol, the occurrence of postoperative complications, the need for additional operations, the development of postoperative new medical conditions (e.g. diabetes mellitus) or the use of GI medications or supplements.

Of the patients who met the inclusion criteria, relevant data were obtained by telephone interviews with willing and cooperative patients who had previously undergone pancreatectomy. Once contact had been established and the purpose of the study stated, in order to assess the QoL of patients in a controlled format, questions were read in a consistent manner from a script. This script included a sequence of corresponding response options from which the patient was required to select an answer. No time constraints were imposed. Responses were promptly recorded.

Before asking the patient about current GI disorders, it was important to establish whether or not the patient had had symptoms prior to his or her diagnosis and whether the patient had developed new, immediately post-surgical symptoms. Patients were first asked about the symptoms they had experienced prior to surgery using an open-ended question format to which the patient could respond by simply listing how he or she had felt or stating that there had been no symptoms. Patients were not asked to recall specific symptoms. Following this, the patient was asked to answer with 'yes' or 'no' according to whether or not the operation had changed the symptoms and then to indicate whether the operation had made these symptoms 'better', 'worse' or caused 'no change'. Lastly, the patient was asked if he or she had developed any new, post-surgical symptoms using an open-ended question format.

Prior to the introductory general open-ended question, the patient was given the Gastrointestinal Symptom Rating Scale (GSRS) to complete during the interview. The GSRS, created in 1988, was originally designed to assess patients with current irritable bowel syndrome and peptic ulcer disease based on previous literature and experiences of pertinent patient symptoms.[6] As a result, this scale assesses five domains that have been identified as important to GI integrity: reflux syndrome; acute pain syndrome; indigestion syndrome; diarrhoea syndrome, and constipation syndrome.[6] Questions within each of these domains assess the intensity, frequency, duration and impact on daily living of each of these syndromes in order to facilitate a comprehensive understanding of various aspects of each syndrome. The GSRS was chosen for this study of pancreatectomy patients because it is a well-validated and reliable questionnaire which refers to and assesses a broad range of GI symptoms.[7] Lower and higher scores imply the presence of less and more severe symptoms, respectively.

Each question within the domain was put to the patient after four response options indicating progressively increasing severity had been read. A score of 0 for a given question indicates that the physiologic impact of the syndrome on that individual is absent or negligible and that negative social effects are absent. A score of 1 indicates that the physiologic impact of the syndrome is noticeable but that negative social impact is absent. A score of 2 indicates that the symptoms have a negative physiologic impact on the patient and a mildly noticeable impact on his or her social performance. Lastly, a score of 3 indicates that the patient experiences great social and activity-related impairment as a result of negative physiologic symptoms.[6,7]

Statistical analysis

All statistical analysis was performed using STATA Version 8.0 (StataCorp LP, College Station, TX, USA). Nominal data were analysed using the chi-squared test. As data from the GSRS were ordinal in nature and therefore non-parametric, these data were analysed using the Mann–Whitney U-test. A P-value of ≤0.05 was considered significant.

Results

Of 169 eligible pancreatectomy patients, 52 were able to be contacted, were qualified to take part in the study and were willing to participate in the telephone survey. Of the remaining 117 patients, 12 were living and unable to be contacted despite repeated attempts to do so and the other 105 had died. Of the participating patients, 30 had undergone a Whipple pancreatectomy, 16 had undergone a distal pancreatectomy, three a central pancreatectomy, two an enucleation, and one a total pancreatectomy. The mean age of the patients was 62.0 ± 13.8 years (range: 24–82 years). Thirty-three (63%) patients were female. With respect to

Table 1 Demographic data for study subjects (n = 52)

Pancreatectomy subtype	
	Whipple, n = 30
	Distal, n = 16
	Central, n = 3
	Enucleation, n = 2
	Total, n = 1
Average age, years	62.0 ± 13.8
Sex, female : male	1.73
Time since pancreatectomy	<2 years, n = 14
	>2 years, n = 38

Table 2 Distribution of pathology in relation to time since pancreatectomy (n = 52)

Pathology	<2 years, n (%)	>2 years, n (%)
Malignant tumours	10 (71%)	17 (45%)
Cystic neoplasms	3 (21%)	14 (37%)
Neuroendocrine tumours	0	4 (11%)
Non-neoplastic benign lesions	1 (7%)	3 (8%)

time elapsed between the pancreatectomy and participating in the survey, 14 of the patients had undergone surgery <2 years prior to completing the GSRS and 38 had undergone surgery >2 years prior to the survey (Table 1). Pathology findings documented that 27 patients had been diagnosed with malignant lesions, 17 patients with cystic lesions, four patients with neuroendocrine tumours, and four patients with non-neoplastic, benign lesions. The distribution of pathology in relation to time elapsed to the survey is represented in Table 2. There was no statistically significant difference in scores for the frequency, severity and duration of symptoms between patients who had undergone surgery >2 years and <2 years, respectively, prior to the survey. The period between the operation and the follow-up survey ranged from 1 year to 13 years.

In response to the question on symptomatic change post-pancreatectomy, 69% of patients reported an overall improvement in preoperative symptoms and 31% reported no change. No patients claimed a worsening of preoperative symptoms. Of the 52 patients, 50% claimed that they had developed new symptoms they had not experienced preoperatively. Of these 50% of patients, 68% had undergone a Whipple operation and 32% had undergone other types of pancreatectomy (P < 0.002).

Scores on three of the five domains on the GSRS (for reflux, constipation and acute pain syndromes) each calculated to a median value of 0 (IQR: 0–1.0). A fourth parameter, indigestion syndrome, generated a median score of 2.0 (IQR: 1.0–4.0). The last parameter, diarrhoea syndrome, also had a median response of 2.0 (IQR: 0.5–4.5) (Table 3). When results were compared for specific operations and their outcomes, patients who had undergone Whipple operations were found to have higher scores in the reflux syndrome and indigestion syndrome domains than patients

Table 3 Scores on the Gastrointestinal Rating Scale (GSRS) (n = 52)

GSRS domain	Median score	Interquartile range
Reflux syndrome	0	0–1.0
Constipation syndrome	0	0–1.0
Acute pain syndrome	0	0–1.0
Diarrhoea syndrome	2.0	0.5–4.5
Indigestion syndrome	2.0	1.0–4.0

who had undergone other types of pancreatectomy, at 0.5 vs. 0 (P = 0.08) and 3.5 vs. 1.5 (P = 0.06), respectively, but these differences did not reach statistical significance.

Discussion

Both pancreatic disease, especially pancreatic cancer, and its treatment affect the patient's QoL in terms of overall general well-being and GI function. Systemic manifestations of pancreatic cancer include fatigue, lassitude, pain, depression and anxiety, among others.[8] These manifestations have been documented using a variety of QoL-related instruments.[9–11] In addition to systemic effects, pancreatic disease manifests specific GI symptoms, such as nausea, vomiting and diarrhoea.[8] Beyond the disease itself, pancreatic resection has been documented to affect overall well-being and QoL.[11–19] Gastrointestinal function and nutritional status are also affected by pancreatectomy.[3,20,21] Even non-resectional procedures affect QoL and symptoms.[22] This study aimed to assess the frequency and magnitude of post-resection GI effects on individuals and to investigate how a patient's life might be influenced both personally and socially as a result of the different types of resection for pancreatic tumours. Understanding these changes and their natural history will allow surgeons to counsel patients more effectively.

More than two-thirds of patients who underwent pancreatectomy experienced some improvement in their preoperative symptoms. Importantly, however, none of the patients found that their preoperative symptoms increased in severity. This is very important because it indicates that pancreatectomy, while of obvious curative intent, also improves the patient's preoperative condition. However, as a result of the alterations to the GI tract and metabolic capacity caused by pancreatectomy, primarily by the Whipple operation compared with the other techniques addressed in this study, half of the patients developed symptoms they had not experienced prior to the operation. It is important to note that, regardless of the post-surgical timeframe, the symptomatic effects remained relatively constant.

With respect to the domains of reflux syndrome (heart burn and acid regurgitation), acute pain syndrome (abdominal pain, hunger pain and nausea) and constipation syndrome (constipation, hard stools and a feeling of incomplete evacuation), the symptoms ranged from virtually non-existent to relatively mild. This is certainly a very positive outcome of which to inform patients prior to surgery. Symptoms in the indigestion syndrome

and diarrhoea syndrome domains ranged from mild to moderate in severity. The indigestion syndrome domain includes the symptoms of abdominal distension, increased flatulence, borborygmus and eructation; patients in this study complained predominantly of the former two symptoms. Symptoms in the diarrhoea syndrome domain consist of loose stools, diarrhoea and urgency of defecation. Again, if the surgical team can acknowledge and appreciate this and make the patient aware of what he or she might expect, they may thereby improve the QoL of that patient through the provision of proper counselling.

It is important to note that many of the patients verbally communicated that they had at times experienced their symptoms with increased severity, and stressed that their dietary intake had significant effects on fluctuations in their symptoms. Patients who claimed to make consistent and appropriate postoperative use of enzymes and particular foods, while avoiding foods known to cause GI problems, acknowledged the importance of this practice in preventing the exacerbation of symptoms. This underlines the necessity of providing the patient with proper dietary counselling in order to lessen the burden of post-surgical GI complications and to improve social outcomes and QoL.

This study has several limitations. Firstly, it represents a cross-sectional analysis of living patients who had no evidence of disease recurrence. Certainly, patients with recurrent or progressive malignancy may have worse symptoms. Secondly, patients in receipt of anti-neoplastic therapy were excluded. Therefore, immediately postoperative patients in this group were not assessed in this study. Thirdly, the data were not gathered prospectively at defined time-points and therefore do not elucidate a natural history of symptomatic change. Fourthly, although the GSRS broadly assesses a wide variety of GI symptoms, it is possible that it did not assess some aspects of QoL and functional status that may be important to patients. In addition, it is difficult to know how reproducible the GSRS is over time. For instance, a patient may give a particular response to a given question during a primary interview and then, in an identical secondary interview conducted after some time has elapsed, may provide a different response to the same question stem and response options. We did not test this variability. The occurrence of diabetes mellitus postoperatively may also affect QoL, but we did not gather information on this issue. Lastly, the sample size was relatively small and therefore some differences in functional status and QoL may have been missed.

Conclusions

In conclusion, many preoperative symptoms are improved by pancreatic resection. Nevertheless, it is common for some new postoperative symptoms to appear. As measured by the GSRS, diarrhoea syndrome and indigestion syndrome appear to be the domains of GI symptoms most affected by pancreatectomy. Nonetheless, the severity of these symptoms appears relatively mild. Pancreatic head resections appear to result in more frequent and possibly more severe symptoms, but, once again, the difference

is relatively small. These results may help surgeons to properly counsel patients on their expected QoL after pancreatectomy.

Conflicts of interest

None declared.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. (2009) Cancer statistics, 2009. *CA Cancer J Clin* 59:225–249.
2. Simons JP, Shah SA, Sing CN, Whalen GF, Tseng JF. (2009) National complication rates after pancreatectomy: beyond mere mortality. *J Gastrointest Surg* 13:1798–1805.
3. Ohtsuka T, Tanaka M, Miyazaki K. (2006) Gastrointestinal function and quality of life after pylorus-preserving pancreaticoduodenectomy. *J Hepatobiliary Pancreat Surg* 13:218–224.
4. Tran TC, van Lanschot JJ, Bruno MJ, van Eljick CH. (2009) Functional changes after pancreaticoduodenectomy: diagnosis and treatment. *Pancreatology* 9:729–737.
5. Menge BA, Schrader H, Breuer TGK, Dabrowski Y, Uhl W, Schmidt WE *et al.* (2008) Metabolic consequences of a 50% partial pancreatectomy in humans. *Diabetologia* 52:306–317.
6. Revicki DA, Wood M, Wiklund I, Crawley J. (1998) Reliability and validity of the Gastrointestinal Symptom Rating Scale in patients with gastroesophageal reflux disease. *Qual Life Res* 7:75–83.
7. Svedlund J, Sjodin I, Dotevall G. (1988) GSRS – a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. *Dig Dis Sci* 33:129–134.
8. Labori KJ, Hjermstad MJ, Wester T, Buanes T, Loge JH. (2006) Symptom profiles and palliative care in advanced pancreatic cancer – a prospective study. *Support Care Cancer* 14:1126–1133.
9. Crippa S, Dominguez I, Rodriguez JR, Razo O, Thayer SP, Ryan DP *et al*. (2008) Quality of life in pancreatic cancer: analysis by stage and treatment. *J Gastrointest Surg* 12:783–794.
10. Velanovich V. (2011) Association of malignancy and survival with quality of life measures in patients with pancreatic pathology. *Pancreas* 40:1063–1069.
11. Pezzilli R, Fantini L, Morselli-Labate AM. (2007) Pancreatectomy for pancreatic disease and quality of life. *JOP* 8 (Suppl. 1):118–131.
12. Huang JJ, Yeo CJ, Sohn TA, Lillemoe KD, Sauter PK, Coleman J *et al*. (2000) Quality of life and outcomes after pancreaticoduodenectomy. *Ann Surg* 231:890–898.
13. Schmidt U, Simunec D, Piso P, Klempnauer J, Schlitt HJ. (2005) Quality of life and functional longterm outcome after partial pancreaticoduodenectomy: pancreaticogastrostomy versus pancreaticojejunostomy. *Ann Surg Oncol* 12:1–6.
14. Billings BJ, Christein JD, Harmsen WS, Harrington JR, Chari ST, Que FG *et al*. (2005) Quality of life after total pancreatectomy: is it really that bad on longterm follow-up? *J Gastrointest Surg* 9:1059–1067.
15. Schniewind B, Bestmann B, Henne-Bruns D, Faendrich F, Kremer B, Kuechler T. (2006) Quality of life after pancreaticoduodenectomy for ductal adenocarcinoma of the pancreatic head. *Br J Surg* 93:1099–1107.
16. Warnick SJ, Velanovich V. (2006) Correlation of patient-derived utility values and quality of life after pancreaticoduodenectomy for pancreatic cancer. *J Am Coll Surg* 202:906–911.
17. Schniewind B, Bestmann B, Kurdow R, Tepel J, Henne-Bruns D, Faendrich F *et al*. (2006) Bypass surgery versus palliative pancreati-

coduodenectomy in patients with advanced ductal adenocarcinoma of the pancreatic head, with an emphasis on quality of life analysis. *Ann Surg Oncol* 13:1403–1411.

18. Parviainen M, Raty S, Nordback I, Sintonen H, Vehkalahti P, Sand J. (2008) Late postoperative quality of life following pancreatic head resections. *Hepatogastroenterology* 55:711–716.

19. Kostro J, Sledzinski Z. (2008) Quality of life after surgical treatment of pancreatic cancer. *Acta Chir Belg* 108:679–684.

20. McLeod RS, Taylor BR, O'Connor BI, Greenberg GR, Jeejeebhoy KN, Royall D *et al*. (1995) Quality of life, nutritional status, and gastrointestinal hormone profile following the Whipple procedure. *Am J Surg* 169:179–185.

21. McLeod RS. (1999) Quality of life, nutritional status, and gastrointestinal hormone profile following the Whipple procedure. *Ann Oncol* 10:281–284.

22. Luman W, Cull A, Palmer KR. (1997) Quality of life in patients stented for malignant biliary obstruction. *Eur J Gastroenterol Hepatol* 9:481–484.